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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/989,695	11/20/2001	Gabriel Lopez-Berestein	UTSC:648US	9730

7590 11/14/2003

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EXAMINER
KISHORE, GOLLAMUDI S

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 11/14/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/989,695	LOPEZ-BERESTEIN ET AL.	
	Examiner	Art Unit	
	Gollamudi S Kishore	1615	

-- Th *MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-32 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-32 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 2-11 and 14-24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The examiner suggests" at least a portion of the lipids is in the form of micelles" in claim 2 and "at least a portion of the lipids is in the form of liposomes" in claim 4.

It should have been "at least one of the lipids is a phospholipid" in claim 3.

The expression, 'imexon or derivative thereof is hydrophobic' in claim 11 is confusing. Isn't imexon water-soluble?

The examiner suggests reciting the chemical names for the compounds in claims 14-24.

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claims 1, 12, 25, 27, 28, 29 and 31-32 are rejected under 35 U.S.C. 102(b) as being anticipated by Hermann (5,369,119).

Hermann discloses compositions containing imexon and a lipid (magnesium stearate) (Example 7).

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 1-2, 12, 25, 27, 28, 29 and 31-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hermann (5,369,119).

The teachings of Hermann have been discussed above. Besides teaching imexon compositions containing the lipid, magnesium stearate, Hermann is suggestive of the use of an oil such as olive oil (oils are lipids) for the administration of imexon (col.4, lines 17-22). Therefore, it would have been obvious to one of ordinary skill in the art to use an oil as a carrier to administer hydrophobic derivatives of imexon or suspension forms or oil micelles with a reasonable expectation of success based on the suggestion of Hermann.

5. Claims 1-2, 11-25, 27-29 and 31-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 99/00120.

WO discloses imexon and several of the claimed derivatives for treating cancer (abstract, pages 3-5). On page 21, WO suggests the use of vegetable oil (lipids)

for the preparation of the slurry of the compounds for administration. Therefore, it would have been obvious to one of ordinary skill in the art to use an oil as a carrier to administer imexon or hydrophobic derivatives of imexon or suspension forms or oil micelles with a reasonable expectation of success based on the suggestion of WO.

6. Claims 1, 3-10, 12, 25 -32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hermann cited above, further in view of either of the references of Sugarman et al (Critical Reviews in Oncology Hematology, 1992 or Ranade (J. Clin Pharmacol., 1989 or Mayer et al (Cancer Letters, 1990) or Weiner et al (Drug development and Industrial Pharmacy, 1989).

The teachings of Hermann have been discussed above. On col. 2, line 58 et seq., Hermann teaches also the use of imexon in combination with other anti-cancer agents. What are lacking in Hermann are the teachings of the use of liposomes as carriers for imexon.

Sugarman while reviewing the use of liposomes as carriers of drugs in the treatment of malignancy teaches that liposomes are sustained release agents and the advantages of their use as carriers of drugs include reduced toxicity associated with those drugs. Sugarman also teaches the use of DMPC/DMPG in a ratio of 7:3. Sugarman further teaches that attachment of monoclonal antibodies to the surface of liposomes to direct the liposomes to the target tissue is known in the art (see entire publication, Introduction and Rationale in particular).

Ranade similarly discloses the advantages of using liposomes as carriers of drugs and their sustained release and site-specific release of drugs (pages 685-691).

Mayer et al teach the tumor uptake and anti-tumor efficacy of doxorubicin against murine mammary tumors (note the summary).

Weiner et al similarly teach the advantages of using liposomes as carriers of drugs and their sustained release and site-specific release of drugs (note Introduction and page 1553).

The use of liposomes as carriers for imexon would have been obvious to one of ordinary skill in the art because of the advantages of liposomes taught by Sugarman, Ranade, Mayer et al and Weiner et al. The criticality of the use of phosphatidylcholine and phosphatidylglycerol with a specific fatty acid chain such as myristic acid is not readily apparent in the absence of unexpected results since these are commonly used phospholipids in the preparation of liposomes as also evident from Sugarman.

7. Claims 1 and 3-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 99/00120, further in view of either of the references of Sugarman et al (Critical Reviews in Oncology Hematology, 1992 or Ranade (J. Clin Pharmacol., 1989 or Mayer et al (Cancer Letters, 1990) or Weiner et al (Drug development and Industrial Pharmacy, 1989).

The teachings of WO have been discussed above. WO also teaches the use of imexon in combination with other anti-cancer agents (page 25). What is lacking in WO is the teaching of the use of liposomes as carriers for the delivery of imexon or its derivatives for the treatment of cancer or stimulating the immune system. It should be noted however that WO teaches the use of slow release carriers on page 22.

As pointed out above, Sugarman while reviewing the use of liposomes as carriers of drugs in the treatment of malignancy teaches that liposomes are sustained release agents and the advantages of their use as carriers of drugs include reduced toxicity associated with those drugs. Sugarman also teaches the use of DMPC/DMPG in a ratio of 7:3. Sugarman further teaches that attachment of monoclonal antibodies to the surface of liposomes to direct the liposomes to the target tissue is known in the art (see entire publication, Introduction and Rationale and Table 1 in particular).

Ranade similarly discloses the advantages of using liposomes as carriers of drugs and their sustained release and site-specific release of drugs (pages 685-691).

Mayer et al teach the tumor uptake and anti-tumor efficacy of doxorubicin against murine mammary tumors (note the summary).

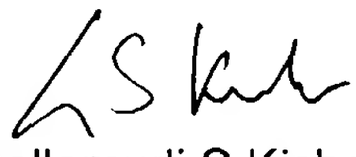
Weiner et al similarly teach the advantages of using liposomes as carriers of drugs and their sustained release and site-specific release of drugs (note Introduction and page 1553).

The use of liposomes as carriers for imexon or its derivatives taught by WO would have been obvious to one of ordinary skill in the art because of the advantages of liposomes taught by Sugarman, Ranade, Mayer et al, and Weiner et al. The criticality of the use of phosphatidylcholine and phosphatidylglycerol with a specific fatty acid chain such as myristic acid is not readily apparent in the absence of unexpected results since these are commonly used phospholipids in the preparation of liposomes as also evident from Sugarman.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gollamudi S Kishore whose telephone number is 703 308 2440. The examiner can normally be reached on 6:30 AM- 4 PM, alternate Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K Page can be reached on 703 308 2927. The fax phone number for the organization where this application or proceeding is assigned is 703 872 9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 308 1234.



Gollamudi S Kishore
Primary Examiner
Art Unit 1615

GSK